

AMENDMENTS TO THE CLAIMS

1. (currently amended) A recombinant herpes simplex virus ~~incapable of~~ expressing only one ~~an active~~ $\gamma_134.5$ gene copy ~~product~~ and comprising an expressible cytokine-encoding DNA.
2. (currently amended) The recombinant herpes simplex virus of claim 1 wherein said virus lacks all or part of a said $\gamma_134.5$ gene copy ~~genes~~.
3. (currently amended) The recombinant herpesvirus of claim 1 wherein said cytokine-encoding DNA is selected from the group consisting of IL-1-, IL-2-, IL-4-, IL-5-, IL-6-, IL-7-, IL-10-, gamma interferon-, granulocyte-macrophage colony stimulating factor, and tumor necrosis factor α encoding DNAs.
4. (currently amended) The recombinant herpes simplex virus of claim 3 wherein said virus comprises a $\gamma_134.5$ gene ~~genes~~ having a deletion of a portion of a coding sequence of said $\gamma_134.5$ gene ~~genes~~; said deletion comprising a Bst EII-StuI fragment of said $\gamma_134.5$ gene ~~genes~~.
5. (currently amended) The recombinant herpes simplex virus of claim 1 wherein said virus comprises a $\gamma_134.5$ gene ~~genes~~ having a stop codon at a Bst EII site in said $\gamma_134.5$ gene ~~genes~~.
6. (currently amended) The recombinant herpesvirus of claim 5 wherein said cytokine-encoding DNA is selected from the group of DNAs consisting of IL-1-, IL-2-, IL-4-, IL-5-, IL-6-, IL-7-, IL-10-, gamma interferon-, granulocyte-macrophage colony stimulating factor, and tumor necrosis factor α encoding DNAs.
7. (original) The recombinant herpes simplex virus of claim 1 wherein said expressible cytokine-encoding DNA is under the promoter-regulatory control of a herpes simplex virus gene promoter.
8. (original) The recombinant herpes simplex virus of claim 7 wherein said herpes simplex virus gene promoter is an EGR-1 promoter.

9. (original) The recombinant herpes simplex virus of claim 1 wherein said cytokine-encoding DNA is under the promoter-regulatory control of a synthetic herpes simplex virus-derived promoter.
10. (original) The recombinant herpes simplex virus of claim 9 wherein said synthetic herpes simplex virus-derived promoter comprises a herpes simplex virus α gene promoter fragment operatively linked 5' to a herpes simplex virus γ gene promoter fragment.
11. (original) The recombinant herpes simplex virus of claim 10 wherein said α gene promoter fragment comprises promoter sequences upstream of the transcription initiation site of the $\alpha 4$ gene and said γ gene promoter fragment comprises a transcription initiation site and the 5' transcribed non-coding sequence of the $\gamma_1\text{UL}19$ gene.
12. (currently amended) The recombinant herpes simplex virus of claim 1 wherein a said $\gamma_1\text{34.5}$ gene copy is ~~genes are~~ replaced by said expressible cytokine-encoding DNA.
13. (original) The recombinant herpes simplex virus of claim 1 wherein said virus comprises two or more copies of said DNA encoding cytokine.
14. (currently amended) A recombinant herpes simplex virus type 1, said virus comprising a DNA encoding IL-4 and expressing only one ~~lacking~~ $\gamma_1\text{34.5}$ gene copy ~~genes~~.
15. (currently amended) The recombinant herpes simplex virus type 1 of claim 14 wherein said IL-4 encoding DNA has replaced a said $\gamma_1\text{34.5}$ gene copy ~~genes~~.
16. (original) The recombinant virus of claim 14 wherein said DNA encoding IL-4 DNA is under the promoter regulatory control of an EGR-1 promoter.
17. (original) The recombinant virus of claim 13 wherein said IL-4 encoding cDNA further comprises a polyadenylation signal.

18. (original) The recombinant virus of claim 14 wherein said polyadenylation signal is a hepatitis B virus-derived polyadenylation signal.

19. (currently amended) A method for treating neoplastic disease ~~of the central nervous system~~, the method comprising administering to a target tumor, a recombinant herpes simplex virus ~~incapable of expressing only one an active~~ $\gamma_134.5$ gene ~~copy product~~ and comprising an expressible cytokine-encoding DNA, wherein the expressed cytokine augments tumor cell killing.

20. (currently amended) The method of claim ~~19~~ 16 wherein said recombinant herpes simplex virus lacks all or part of ~~a said~~ $\gamma_134.5$ gene copy genes.

21. (currently amended) The method of claim 20 wherein said cytokine-encoding DNA is selected from the group of DNAs consisting of IL-1-, IL-2-, IL-4-, ~~IL-5-~~, IL-6-, IL-7-, ~~IL-10-~~, gamma interferon-, granulocyte-macrophage colony stimulating factor, and tumor necrosis factor- α encoding DNAs.

22. (currently amended) The method of claim ~~19~~ 16 wherein said recombinant herpes simplex virus comprises ~~a~~ $\gamma_134.5$ gene genes having a stop codon at a Bst EII site in said $\gamma_134.5$ gene genes.

23. (currently amended) The method of claim 22 wherein said cytokine encoding DNA is selected from the group of DNAs consisting of IL-1-, IL-2-, IL-4-, ~~IL-5-~~, IL-6-, IL-7-, ~~IL-10-~~, gamma interferon-, granulocyte-macrophage colony stimulating factor, and tumor necrosis factor- α encoding DNAs.

24. (currently amended) The method of claim 19 wherein said recombinant herpes simplex virus comprises ~~a~~ $\gamma_134.5$ gene genes lacking a portion of the coding sequence corresponding to a Bst EII/StuI restriction fragment of said $\gamma_134.5$ gene genes.

25. (original) The method of claim 19 wherein said expressible cytokine-encoding DNA is under the promoter-regulatory control of a herpes simplex virus gene promoter.

26. (currently amended) The method of claim ~~25~~ 23 wherein said herpes simplex virus promoter is an EGR-1 promoter.

27. (original) The method of claim 19 wherein said cytokine-encoding DNA is under the promoter regulatory control of a synthetic herpes simplex virus derived promoter.

28. (original) The method of claim 27 wherein said synthetic herpes simplex derived promoter comprises a herpes simplex virus α gene fragment operatively linked 5' to a herpes simplex virus γ gene promoter fragment.

29. (original) The method of claim 28 wherein said α gene promoter fragment comprises promoter sequences upstream of the transcription initiation site of said α gene promoter fragment comprises the transcription initiation site and the 5' transcribed non-coding sequence of the γ_1 U_L19 gene.

30. (currently amended) The method of claim 20 wherein said γ_1 34.5 gene is genes are replaced by said expressible cytokine-encoding DNA.

31. (currently amended) A pharmaceutical composition comprising in a pharmaceutically acceptable carrier, diluent, or adjuvant, a recombinant herpes simplex virus ~~incapable of expressing~~ only one an active γ_1 34.5 gene copy product, said virus comprising an expressible cytokine-encoding DNA, wherein the expressed cytokine augments tumor cell killing.

32. (canceled)

33. (new) The method of claim 19, wherein the target tumor is a tumor of the central nervous system.